NFA 305 (Dockets Management Bl)

Date of Approval Letter:

DEC 2 1998

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 110-048

VALBAZEN® (albendazole)

"....for the removal and control of a variety of internal parasites common in cattle and sheep."

Sponsored by: Pfizer, Inc.

VALBAZEN® General Information

I. GENERAL INFORMATION

NADA Number: 110-048

Sponsor: Pfizer, Inc.

235 East 42d Street

New York, New York 10017

Established Name: albendazole

Trade Name: VALBAZEN®

Pharmacological category: antiparasitic

How Supplied: 500- and 1000-mL bottles

Label claim of the Amount of Active Ingredient(s):

11.36% suspension (113.6 mg/mL)

Marketing Status: over-the-counter

Species: sheep and cattle

Effect of the Supplement: The supplement adds sheep uses approved for a less

concentrated suspension to labeling for an approved,

more concentrated formulation.

II. INDICATIONS FOR USE

For the removal and control of the following parasites in cattle and sheep

Parasite	Cattle	Sheep
Liver Flukes	Fasciola hepatica	Fasciola hepatica, Fascioloides magna
Tapeworms (heads and segments)	Moniezia benedeni, M. expansa	Common Tapeworms (Moniezia expansa), Fringed Tapeworms (Thysanosoma actinioides)
Stomach Worms (adults and 4* stage larvae)	Brown Stomach Worms, including 4th stage inhibited larvae (Ostertagia ostertagi), Barberpole Worms (Haemonchus contortus, H. placei), Small Stomach Worms (Trichostrongylus axei)	Brown Stomach Worms (Ostertagia circumcincta, Marshallagia marshalli), Bark-pole Worms (Haemonchus contorts), Small Stomach Worms (Trichostrongylus axei)

VALBAZEN® Dosage Form

Intestinal Worms (adults and 4th stage larvae)

Thread-Necked Intestinal Worms (Nematodirus spathiger, N. helvetianus), Small Intestinal Worms (Cooperia oncophora, C. punctata)

Thread-Necked Intestinal
Worms (Nematodirus
spathiger, N. filicollis),
Cooper's Worm (Cooperia
oncophora), Bankrupt Worms
(Trichostrongylus
colubriformis), Nodular Worms
(Oesophagostomum
columbianum), Large-Mouth
Bowel Worms (Chabertia
ovina)

Intestinal Worms (adults and **4**th *stage* larvae)

Hookworms (Bunostomum phlebotomum), Bankrupt Worms (Trichostrongylus colubriformis), Nodular Worms (Oesophagostomum radiatum)

Lungworms (adults and 4th stage Dictyocaulus viviparus

larvae)

Lungworms (adults and larval *stages*)

Dictyocaulus filaria

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

A. *Dosage Form:* suspension

B. Route of Administration: oral, as a drench

C. *Recommended Dosage:* 7.5 mg/kg body weight (3.4 mg/lb; sheep) or 10 mg/kg body weight (4.45 mg/lb; cattle).

IV. TARGET ANIMAL SAFETY AND EFFECTIVENESS

Target animal safety and effectiveness data for albendazole in sheep and cattle were accepted under original NADA 140-934& NADA 110-048.

The increased albendazole concentration is not expected to pose any specific risk hazard to sheep. The actual amount of drug administered to sheep per unit body weight remains unchanged. CVM has concluded that the two formulations should perform in an identical manner when administered to sheep. Accordingly, the sponsor's request for waiver of *in vivo* study requirement has been granted, and no additional studies are required to support the approval of the 11.36% oral suspension of albendazole for sheep.

VALBAZEN® Human Safety

VI. HUMAN SAFETY

This supplemental NADA did not require new human safety studies. The basic toxicology and residue chemistry studies that support the use of albendazole in cattle and sheep are summarized in the FOI Summaries for the original approvals of albendazole under NADA 110-048 and NADA 140-934. Based on the original NADAs, the following has been assigned to this product:

- a. Acceptable Daily Intake: The Acceptable Daily Intake (ADI) of 5 μg/kg body weight/day was assigned to cattle and sheep on the basis of the toxicology studies.
- b. Safe Concentrations of Residues: The safe concentrations of albendazole residues in edible tissues of sheep and cattle were established at 0.6 part per million(ppm) for sheep and cattle muscle, 3.0 ppm for liver, kidney and fat tissue of sheep, 1.2 ppm for cattle liver, 1.8 ppm for cattle kidney, and 2.4 ppm for cattle fat.
- c. *Tolerances of Marker Residue:* Residue and metabolism studies established 0.2 ppm and 0.25 ppm as the tolerances for residues of albendazole 2-aminosulfone (the marker residue) in cattle liver (target tissue) and sheep liver, respectively.
- d. Assignment of a muscle tolerance: A tolerance of 0.05 ppm albendazole 2-aminosulfone is assigned for cattle and sheep muscle following a review of the residue studies conducted with albendazole in those species. The total residue studies conducted with ¹⁴C-albendazole show that total residues in muscle are expected to be in the range of 1 ppm to 4 ppm at 1 day after dosing under the approved conditions of use and that those residues deplete to 0.06 ppm or less (1 0°/0 of the 0.6 ppm muscle safe concentration) by 3 to 4 days after dosing. Because of the rapid depletion of total residues from muscle, muscle tissue was not assayed in any of the non-radiolabeled (withdrawal) residue studies in either NADA 110-048 or NADA 140-934. Likewise, the metabolizes present in muscle were not profiled.

With a minimum of residue data available, the muscle tolerance value is estimated with consideration given to the metabolize profile data in liver of each species and to the capabilities of the determinative analytical method for residues in liver. A concentration of 0.05 ppm of the marker residue is assigned as the muscle tolerance because it represents a conservative estimate of the tolerance, and it is above the 0.025 ppm limit of quantitation of the determinative assay as validated in liver. The 0.05 ppm muscle tolerance makes it possible toidentify cattle or sheep that have been marketed within 1 to 3 days after treatment with albendazole. As withdrawal times approaching the preslaughter withdrawal periods of 27 days for cattle and 7 days for sheep, the marker residue is unlikely to be detected in muscle tissue.

VALBAZEN® Agency Conclusions

VII. AGENCY CONCLUSIONS

The information submitted in support of this application comply with the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 5 14) and indicate that albendazole oral suspension (1 1.36°/0) is safe and effective in sheep for the conditions of the use described in labeling.

Although no new toxicology or residue chemistry studies were submitted with this supplement, CVM has used this opportunity to assign a tolerance of 0.05 ppm albendazole 2-aminosulfone for residues of albendazole in cattle and sheep muscle. The pre-slaughter withdrawal periods of 27 days in cattle and 7 days in sheep remain unchanged.

There is reasonable certainty that the directions for use on labeling can and will be followed in practice. Accordingly, the Agency has concluded that this product shall retain **over-the**-counter marketing status.

In accordance with 21 CFR 514.106(b)(2), this is a category II change which did not require a reevaluation of the safety and effectiveness data in the parent application.

The Agency has **carefully** considered the potential environmental effects of this action and has concluded that the action qualifies for a categorical exclusion from the requirement to prepare an environmental assessment in accordance with 21 CFR 25.33(a)(l).

VIII. APPROVED LABELING (attached)

Facsimile label. 1-liter bottle



(albendazole)

Broad-Spectrum **Dewormer**

Oral Suspension for Use in Cattle and Sheep

Controls:

Stomach Worms including 4th stageinhibited larvae of Ostertagia ostertagi

Intestinal Worms

Lungworms

Tapeworms

Mature Liver Fluke

1 L/33.8 fl 02 (1 qt 1.8 fl 02)

NADA #1 10-048, Approved by FDA

889 85-8784-05



4 I/4"(W) x 4 1/2"(H)









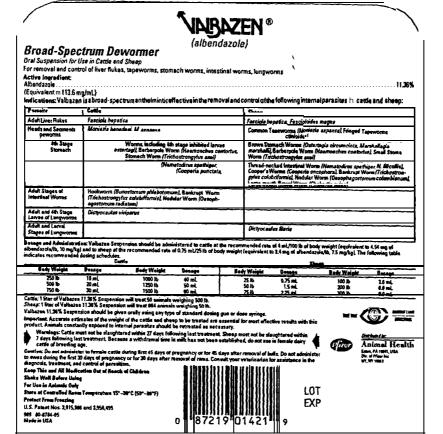
PMS 116

PMS 2415

Black

60% Black

85-8784-05 Draft #1 9/2/98



4 1/4"(W) x 4 1/2"(H)

EXP



Black

80-8784-05 Draft #1 9/1/?38



Broad-Spectrum Dewormer

Oral Suspension for Use in Cattle and Sheep

For removal and control of liver flukes, tapeworms, stomach worms, intestinal worms, lungworms

Active Ingredient

Albendazole...

(Equivalent to 113.6 mg/mL)

Indications: Valbazen is a broad-spectrum anthelmintic effective in the removal and control of the following internal parasites in cattle and sheep

Parasite	cattle	Sheep
Adult liver Flukes	Fasciola hepatica	Fasciola hepatica, Fascioloides magna
Heads and Segments of Tapeworms	Moniezia benedeni, M. expansa	Common Tapeworms (Moniezia expansa), Fringed Tapeworms (Thysanosoma actinioides)
Adult and 4th Stage Larvae of Stomach Worms	Brown Stomach Worms, including 4th stage inhibited larvae (Ostertagia ostertagii), BarberPole Worm (Haemonchus contortus, H. placei), Small Stomach Worm (Trichostrongylus axei)	Brown Stomach Worms (Ostartagia circumcinta, Marshallagia marshalli), Barberpole Worm (Haemonchus contortus), Small Stomach Worm (Trichostrongylus axei)
Adult arrd 4th Stage larvae of Intestinal Worms	Thread-necked Intestinal Worm (Nematodirus spathiger, N. helvatianus), Small intestinal Worm (Cooperia punctata, C oncophora)	Thread-necked Intestinal Worm (Nematodirus spathiger, N. filicollis), Cooper's Worms (Cooperia oncophora), Bankrupt Worm (Trichostron- gylus colubriformis), Nodular Worm (Oesophagostomum columbianum), Large-mouth Bowel Worm (Chabertla ovina)
Adult Stages of Intestinal Worms	Hookworm (Bunostomum phlebotomum), Bankrupt Worm (Trichostrongylus colubriformis), Nodular Worm (Oesophagostomum radiatum)	
Adult and 4th Stage Larvae of Lungworms	Dictyocaulus viviparus	
Adult and Larval Stages of Lungworms		Dictyocaulusfilaria

Desage and Administration: Valbazen Suspension should be administered to cattle at the recommended rate of 4mL/100 lb of body weight (equivalent to 4.S4 mg of albendazole/lb, 10 mg/kg) and to sheep at the recommended rate of 0.75 ml/25 lb of body weight [equivalent to 3.4 mg of albendazole/lb, 7.5 mg/kg). The following table indicates recommended dosing schedules.

Cattle				Sheep					
Ξ	Body Weight	Dosage	Body Weight	Dosage	Body Weight	Dosage	Body Weight	Dosage	
_	250 lb	10 mL	1000 lb	40 mL	25 lb	0.75 mL	100 lb	3.0 mL	
	500 lb	20 mL	1250 lb	50 mL	50 lb	1.5 mL	200 lb	6.0 mL	
	750 lb	30 mL	1500 lb	60 mL	i 751b	2.25 ml	300 th	9.0 ml	

Cattle: 1 liter of Valbazen 11.36% Suspension will treat 50 animals weighing 500 lb. Sheep: 1 liter of Valbazen 11.36% Suspension will treat 664 animals weighing 50 lb.

Valbazen 11.36% Suspension should be given orally using any type of standard dosing gun or doss syringe.

Important: Accurate estimates of the weight of the cattle end sheep to be treated are essential for most effective results with this product Animals constantly exposed to internal parasites should be recreated es necessary,

Warnings Cattle must not be slaughtered within 27 days following last treatment Sheep must not be slaughtered within 7 days following fast treatment Because a withdrawal tima in milk has not been established, do not use in female dairy

cattle of breeding age.

Caution: Do not administer to female cattleduring first 45 days of pregnancy or for 45 days after removal of buffs. Do not administer to ewes during tha first SO days of pregnancy or for 30 days after removal of rams. Consult your veterinarian for assistance in the diagnosis, treatment. and control of parasitism.

Keep Thk and All Medication Out of Reach of Children

Shake Well Before Using For Use in Animals Only

Store at Controlled Room temperature 15--SO-C (59°-86°F)

protect From Freezing

U.S. Patent Nos. 3,915,%6 and 3,%6,498

86S **80-8784-05** Made in USA



Animal Health Enton PA 19341, USA Div. d Prizer Inc. NY,NY 10017

LOT **EXP**

1 50%

 $4\frac{1}{4}$ "(W) x $4\frac{1}{2}$ "(H)



Black

80-8784-05 Draft #1 9/1/98